Author’s response to reviews

Title: Prevalence and risk factors for chronic kidney disease of unknown cause in Malawi: a cross-sectional analysis in a rural and urban population

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Author’s response to reviews:

Dear Dr Henderson,

We thank you for your consideration of this manuscript "Prevalence and risk factors for chronic kidney disease of unknown cause in Malawi: a cross-sectional analysis in a rural and urban population" (BNEP-D-19-01054).

We appreciate your suggestions, which have been helpful in improving the manuscript, and we thank the reviewers for their additional comments.

All the comments we received have been addressed in order to improve the quality of our article, and we present our reply to each of them separately.

Reviewer comments are in parentheses, and our responses are below each comment.
Comments from Reviewer 1:

1. “Abstract: The meaning of the last sentence of the results section of the abstract is unclear. Suggest change to "No increased risk of eGFR<90 was observed for rural participants."”

Response: We agree with this suggestion and have made the necessary changes in the abstract

2. “Page 9, row 35: units for FFM should be kg, not kg/m2”

Response: this has been noted and changed

3. “Throughout the paper, when eGFR as a continuous variable is discussed (e.g. Page 11, row 13-14; Page 12, row 1) it would be better for clarity to refer to "lower" rather than "reduced" eGFR. When eGFR<90 is discussed the term "reduced" is more appropriate.”

Response: We agree with this and have made the changes to the terminology between “lower” and “reduced” eGFR throughout the manuscript

Comments from Reviewer 2:

1. “The authors did not address my comment regarding exclusion criteria. The CKDu definition used in this study is not correct (because of the exclusion of individuals with a single blood pressure measurement ≥140/90 mmHg while CKDu definition requires to exclude those with a history of hypertension treated with at least 2 anti-hypertensive drugs or BP≥160/100) and led to the selection of individuals with normal kidney function.”

Response: We have now clarified in the text that there is currently no globally accepted definition for CKDu, and that there are region-specific differences in exclusion criteria (notably hypertension cut-offs) when assessing CKDu (outside of the DEGREE protocol). DEGREE have used a more conservative definition of CKDu and cut-off values so as not to overestimate the prevalence of disease in suspected high-risk regions. Previous studies in India, Sri Lanka and Central America have used both the DEGREE definitions and region-specific definitions, all of which found a substantial burden of the disease when using both the regional definitions and more conservative DEGREE definitions.
2. “This study does not provide any new meaningful information regarding CKDu in this world region and confirms previous negative findings in the same population (Nakanga et al, 2019).”

Response: We have made changes to the manuscript when addressing the Nakanga study in order to make it explicit what the differences are between this KDU study and the Nakanga study. We have added that the Nakanga study did not use the DEGREE diagnostic definitions, and that as the Malawian population are “suspected” to be at higher risk of CKDu based on a priori hypotheses, this warranted further study in this population using the new and standardized method of measurement of eGFR and DEGREE diagnostic definitions.

The reviewers’ second revision of the manuscript and suggestions have been very helpful, and we hope that these changes we have made will facilitate the decision to publish this article in your journal.

We are open to consideration of any further comment on our answers.

Kind regards,

Sophie Hamilton